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CERTIFICATE OF MAILING 37 C.F.R. 1.8	
I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on the date below:	
12/3/03 November 12, 2003 Date	 David L. Parker

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Wold *et al.*

Serial No.: 09/351,778

Filed: July 12, 1999

For: Replication Competent Anti-Cancer Vectors

Group Art Unit: 1632

Examiner: Priebe, Scott David

Atty. Dkt. No.: 66153-7775

SUPPLEMENTAL DECLARATION OF THE INVENTORS UNDER 37 C.F.R. §1.131

We, William S.M. Wold, Ann E. Tollefson, Konstantin Doronin and Karoly Toth, declare as follows:

1. We are joint inventors of the subject matter claimed in the referenced patent application. We are submitting the present §131 declaration to supplement our earlier declaration filed January 6, 2003, the contents of which are incorporated herein by reference.
2. In our earlier declaration we demonstrated that the adenovirus vector KD1 was constructed prior to March 3, 1997, and, in numerous studies that we conducted between 5/9/97 and 6/2/97, KD1 was shown to overexpress ADP. We are submitting the present Supplemental Declaration to supplement our earlier declarations by demonstrating that (1) prior to March 3, 1997, we conceived of using ADP-expressing adenoviral vectors for treating cancer in patients,

and that (2) shortly after March 3, 1997 an exemplary vector, KD1, was tested in an animal having cancer and shown to have anticancer activity.

3. Prior to March 3, 1997 we conceived of the idea of using adenovirus vectors expressing the ADP gene as a therapeutic agent to treat cancer. This is shown, for example, in the exhibits to our 1/6/03 declaration, in particular, Exhibit B at, for example, page 3, section B, and pages 4-8. The Exhibit B document is dated prior to March 3, 1997.

4. On July 7, 1997, we sent KD1, dl1101/1107, dl309, and A549 cells to Dr. Jeffrey A. Whitsett at the Children's Hospital Medical Center, Division of Pulmonary Biology, Cincinnati, OH. A copy of the cover letter sent to Dr. Whitsett is attached as Exhibit M. Dr. Whitsett had agreed to test these vectors on our behalf in the A549 nude mouse model, in which A549 human lung carcinoma cells are used to establish tumors in nude mice following by injection of the various vectors to determine their anticancer efficacy. On September 16, 1997, we received a report from Dr. Whitsett's colleague, Lee Zhang, indicating that "10⁹ pfu of each of the viruses were injected into each established A549 tumor. 4 out of 6 tumors injected with KD1 showed slowed tumor growth while 2 out of 2 tumors injected with dl309 and 4 out of 4 injected with dl 1101/1107 continued to grow." A copy of this fax is attached as Exhibit N.

5. Accordingly, foregoing studies conducted on our behalf demonstrated the successful use of KD1 in the treatment of cancer in an animal at least as early as September, 1997.

6. We hereby declare that all statements made of our own knowledge are true and all statements made on information are believed to be true and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or

imprisonment or both under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issued thereon.

December 1, 2003
Date

William S.M. Wold
William S.M. Wold

December 1, 2003
Date

Ann E. Tollefson
Ann E. Tollefson

December 1, 2003
Date

Konstantin Doronin
Konstantin Doronin

December 1, 2003
Date

Karoly Toth
Karoly Toth

7/8/97

Dear Jeff:

- Please find enclosed:

dl309, 2.15×10^{10} PFU/ml, ~ 200 μ l

dl1101/1107, 1.95×10^{10} PFU/ml, 2 ml

KD1, 9×10^{10} PFU/ml, 2 ml

A549 cells, passage 78.

- dl309 is Ad5, with the E3 10.4k, 14.5k, 14.7k genes ^{deleted}
- dl1101/1107, deletes the RB and p300 binding sites required to drive cells from G₀ \rightarrow S phase, in dl309 ^{backbone}
- KD1, is in dl1101/1107 background.

Lacks all E3 (stealth) genes. Engineered to overexpress the Adenovirus Death Protein (ADP).

- Bill

FAX MESSAGE

DATE 9/16/97

TO

Name Bill Wald

Address _____

Fax Number 314 713 3403 Phone Number _____

Number of pages (including this one): 1

MESSAGE: 10⁷ pfu of adenovirus were injected into each established A349 tumor. 4 out of 6 tumors injected with KD1 showed slowed tumor growth. While 2 out of 2 tumors injected with dl 309 and 4 out of 4 injected with dl 1101/1107 continued to grow.

FROM

Name Lee Zhang

CHILDREN'S HOSPITAL MEDICAL CENTER
DIVISION OF NEONATOLOGY
3333 Burnet Avenue
Cincinnati, Ohio 45229-3039
Phone (513) 636-7992
Fax (513) 636-7868